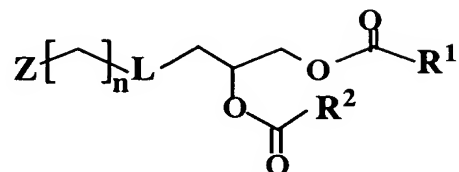


IT IS CLAIMED:

1. A liposome composition, comprising:  
a lipid having the formula



where each of  $\text{R}^1$  and  $\text{R}^2$  is an alkyl or alkenyl chain having between 8-24 carbon atoms, and each of  $\text{R}^1$  and  $\text{R}^2$  are independently selected;

$n = 0-20$ , preferably  $n = 1-20$ ;

L is selected from the group consisting of (i)  $-\text{X}-(\text{C}=\text{O})-\text{Y}-$ , (ii)  $-\text{X}-(\text{C}=\text{O})-$ , and (iii)  $-\text{X}-$ , where X and Y are independently selected from oxygen, NH and a direct bond;

Z is a weakly basic moiety that has a pK of less than 7.4 and greater than about 4.0.

2. The composition of claim 1, wherein X is NH and Y is oxygen.
3. The composition of claim 1, wherein L is a carbamate linkage, an ester linkage or a carbonate linkage.
4. The composition of claim 1, wherein L is  $\text{NH}-(\text{C}=\text{O})-\text{O}-$ .
5. The composition of claim 1, wherein Z is an imidazole.
6. The composition of claim 1, comprising between 1-80 mole percent of the lipid.
7. The composition of claim 1, wherein Z is a moiety having a pK value between 5.0-6.5.

8. The composition of claim 1, wherein each of R<sup>1</sup> and R<sup>2</sup> is an unbranched alkyl or alkenyl chain having between 8-24 carbon atoms.

9. The composition of claim 8, wherein each of R<sup>1</sup> and R<sup>2</sup> is C<sub>17</sub>H<sub>35</sub>.

10. The composition of claim 1, wherein n is between 1-10.

11. The composition of claim 1, further including a therapeutic compound entrapped in the liposomes.

12. The composition of claim 11, wherein the therapeutic agent is a nucleic acid.

13. The composition of claim 12, wherein the nucleic acid is selected from DNA, RNA, fragments thereof and oligonucleotides.

14. The composition of claim 1, further including a ligand for targeting the liposomes to a target site.

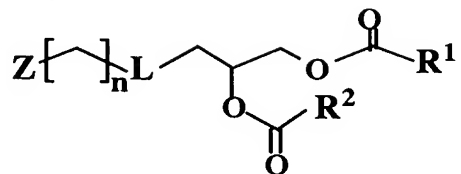
15. The composition of claim 14, wherein the ligand is one having binding affinity for endothelial tumor cells and which is internalized by such cells.

16. The composition of claim 15, wherein the ligand is selected from the group consisting of E-selectin, Her-2 and FGF.

17. The composition of claim 1, wherein said liposomes further include between 5-20 mole percent of a vesicle-forming lipid derivatized with a hydrophilic polymer chain.

18. The composition of claim 17, wherein said hydrophilic polymer chain is polyethyleneglycol.

19. A lipid having the formula:



where each of  $\text{R}^1$  and  $\text{R}^2$  is an alkyl or alkenyl chain having between 8-24 carbon atoms, and each of  $\text{R}^1$  and  $\text{R}^2$  are independently selected;

$n = 0-20$ , preferably  $n = 1-20$ ;

L is selected from the group consisting of (i)  $-\text{X}-(\text{C}=\text{O})-\text{Y}-$ , (ii)  $-\text{X}-(\text{C}=\text{O})-$ , and (iii)  $-\text{X}-$ , where X and Y are independently selected from oxygen, NH and a direct bond;

Z is a weakly basic moiety that has a pK of less than 7.4 and greater than about 4.0.

20. The lipid of claim 19, wherein X is NH and Y is oxygen.

21. The lipid of claim 19, wherein L is a carbamate linkage, an ester linkage or a carbonate linkage.

22. The lipid of claim 19, wherein L is  $\text{NH}-(\text{C}=\text{O})-\text{O}-$ .

23. The lipid of claim 22, wherein Z is an imidazole.

24. The lipid of claim 19, wherein Z is a moiety having a pK value between 5.0-6.5.

25. The lipid of claim 19, wherein each of  $\text{R}^1$  and  $\text{R}^2$  is an unbranched alkyl or alkenyl chain having between 8-24 carbon atoms.

26. The lipid of claim 23, wherein each of  $\text{R}^1$  and  $\text{R}^2$  is  $\text{C}_{17}\text{H}_{35}$ .

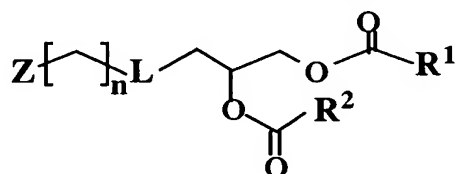
27. The lipid of claim 19, wherein n is between 1-10.

28. A liposome comprising the lipid according to claim 19.

29. A liposome comprising the lipid according to claim 26.

30. A method for delivery of a therapeutic agent to the cytoplasm of a cell, comprising

preparing liposomes comprising a lipid having the formula



where each of  $\text{R}^1$  and  $\text{R}^2$  is an alkyl or alkenyl chain having between 8-24 carbon atoms, and each of  $\text{R}^1$  and  $\text{R}^2$  are independently selected;

$n = 0-20$ , preferably  $n = 1-20$ ;

L is selected from the group consisting of (i)  $\text{---X---(C=O)---Y---}$ , (ii)  $\text{---X---(C=O)---}$ , and (iii)  $\text{---X---}$ , where X and Y are independently selected from oxygen, NH and a direct bond;

Z is a weakly basic moiety that has a pK of less than 7.4 and greater than about 4.0; and

administering the liposomes to a subject.

31. The method of claim 30, wherein said preparing includes entrapping in the liposomes a nucleic acid.

32. The method of claim 31, wherein the nucleic acid is an oligonucleotide.

33. The method of claim 30, wherein said preparing includes entrapping in the liposomes a protein.